## REMARKS

Applicants would like to thank the Examiner for carefully reading the subject application and for suggesting claim amendments to overcome the rejections under 35 U.S.C. §112, second paragraph.

Claim amendments

Claim 1 has been amended to provide proper antecedent basis and to indicate that the cells in step e) have been "re-sorted". Support for the amendment can be found, for example, on page 6, lines 16 and 26-27 and in Figure 1 of the specification.

Claims 6 and 56 have been amended to indicate that the method comprises the additional step of stimulating the cells with insulin. Support for the amendment can be found, for example, on page 59, lines 26-28 of the specification.

Claim 15 has been amended to provide proper antecedent basis and to add a step of stimulating cells with insulin. Support for the amendment can be found, for example, on page 7, line 19 of the specification.

Claim 25 has been amended to include the steps of "isolating the enriched library" and "introducing the enriched library into cells" after step a). Support for the amendment can be found, for example, on page 20, lines 18-24 of the specification.

Claim 55 has been amended to be rewritten in independent format. Support for the amendment can be found, for example, in original Claim 54.

Claim 57 has been amended to include 2 steps of insulin stimulation of cells. Support for the amendment can be found, for example, on page 6, lines 16 and 26-27 and page 59, lines 26-28.

No new matter has been added.

Oath/Declaration

The Examiner states that the oath or declaration is defective "because [n]on-initialed and/or non-dated alterations have been made to the oath or declaration", and thus, requires a new oath or declaration (Office Action, page 2).

A Supplemental Declaration executed by Jonathan S. Bogan is being filed concurrently.

Rejection of Claims 1-21, 25-31, 56 and 57 under 35 U.S.C. §112, second paragraph

Claims 1-21, 25-31, 56 and 57 are rejected under 35 U.S.C. §112, second paragraph "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention" (Office Action, page 3).

The Examiner states that "Claim 1 is vague and indefinite in that there is no clear and positive prior antecedent basis in the claims for newly added steps (d), (e) and (f)" and suggests amending "step (d) to refer to the cells sorted in step (c), step (e) to refer to the cells expanded in step (d) and step (f) to refer to the cells sorted in step (e)" (Office Action, page 3). The Examiner states that "Claim 1 is additionally vague and indefinite because step (e) recites sorting of cells that have been expanded, but there is no basis for this sorting" and suggests amending Claim 1 to clearly state that "the cells were re-sorted to ensure purity of the sorted populations" (Office Action, page 3).

Claim 1 has been amended in accordance with the Examiner's suggested claim amendments.

The Examiner states that "Claims 6 and 56 are vague and indefinite because to repeat the sorting and expansion steps one must first stimulate with insulin" and suggests amending the claims to "include stimulation with insulin in the additional steps recited" (Office Action, page 3).

Claims 6 and 56 have been amended in accordance with the Examiner's suggested claim amendment.

The Examiner states that "Claim 15 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term 'the population of cells' recited in step (e)" and that "[i]t would seem that an insulin stimulation step is necessary prior to step (h)" (Office Action, page 4).

Claim 15 has been amended to delete the step of "subdividing the population of cells into pools of cells such that each pool is a subset of the population of cells" and to add a step of stimulating the cells which comprise DNA encoding a protein involved in GLUT4 trafficking and the GLUT 4 reporter protein with insulin, in order to more clearly recite the claimed method.

The Examiner states that "Claim 25 is vague and indefinite because multiple expression libraries are referred to without clearly identifying which library is the intended" and suggests replacing "the expression library" in line 3 of step (a) with "an expression library" (Office Action, page 4). In addition, the Examiner states that "the library of step (b) lacks a positive antecedent basis" and suggests replacing "the library" with "the enriched library" (Office Action, page 4). Finally, the Examiner states that "Claim 25 is further vague and indefinite because the preamble of step (a) recites that an enriched expression library is being prepared, but the end product are cells comprising an expression library" and suggests amending the claim to recite steps where the library is isolated and then introduced to cells prior to step (b) (Office Action, page 4).

Claim 25 has been amended in accordance with the Examiner's suggested claim amendments.

The Examiner states that "Claim 57 is vague and indefinite because there is no basis for sorting cells in either step (a) or step (c)" and suggests amending the claim to insert steps reciting insulin stimulation prior to steps (a) and (c) (Office Action, page 4).

Claim 57 has been amended in accordance with the Examiner's suggested claim amendment.

As amended, the claims are definite and particularly point out and distinctly claim the subject matter which Applicants regard as the invention

Rejection of Claims 1, 10, 11, 15, 20, 21, 30, 31, 54 and 57 under the judicially created doctrine of obviousness-type double patenting

Claims 1, 10, 11, 15, 20, 21, 30, 31, 54 and 58 are rejected under the judicially created doctrine of obviousness-type double patenting "as being unpatentable over claims 23, 28 and 29 of U.S. Patent No. 6,632,924 in view of Seed" (Office Action, page 5). Specifically the Examiner states that "the patent claims are drawn to a method for identifying 'an agent' which is involved in GLUT4 trafficking to the plasma membrane" and "do not address using an expression library as the 'agent' as the instant claims do" (Office Action, page 5). The Examiner cites Seed as teaching "the well-known process of expression cloning for the identification of new genes in a signaling pathway" (Office Action, page 5). The Examiner states that "the instant

claims are essentially drawn to method of expression cloning for the identification of proteins involved in GLUT4 trafficking to the plasma membrane" and that "the skilled artisan would have been motivated to perform expression cloning to identify novel proteins in the process of GLUT4 trafficking to the plasma membrane utilizing expression libraries as the 'agent' of the patent claims" (Office Action, page 6).

Applicants respectfully disagree. Applicants' invention is directed to methods useful for identification and isolation of ***proteins involved in insulin stimulated GLUT4 trafficking***. Specifically, Applicants' claimed invention is directed to methods of enriching an expression library wherein the expression library comprises DNA encoding a protein involved in insulin stimulated GLUT4 trafficking at the plasma membrane (Claims 1, 54 and 57) and methods for identifying a protein involved in insulin stimulated GLUT4 trafficking at the plasma membrane (Claims 15 and 25). In order to enrich the expression libraries and identify proteins involved in insulin stimulated GLUT4 trafficking, the methods include a step in which cells comprising an expression library comprising DNA encoding a protein involved in GLUT4 trafficking at the plasma membrane ***are stimulated with insulin*** (Claim 1, step b; Claim 15, step c; Claim 25, step a; Claim 54; Claim 57, steps a and d). Cells which comprise an altered proportion of GLUT4 at the cell surface upon stimulation with insulin comprise proteins involved in GLUT4 trafficking at the plasma membrane.

Claim 23 of U.S. Patent No. 6,632,924 (the '924 Patent) is directed to a "method of identifying an agent which enhances translocation of GLUT4 from an intracellular location in [to] the plasma membrane in mammalian cells" (Claim 23, preamble). The method comprises culturing cells which express a modified GLUT4 which comprises at least one epitope tag in an extracellular domain and a fluorescent tag in an intracellular domain in the presence of a candidate agent. A relative proportion of the modified GLUT4 protein at the plasma membrane of the cells to the total modified GLUT4 protein in the cells is determined and compared to a control value. If the test value is greater than the control value, then the candidate agent is an agent which enhances translocation of GLUT4 from an intracellular location to the plasma membrane in mammalian cells.

In contrast to Applicants' claimed invention, in the claimed method of the '924 Patent, the cells are ***not*** stimulated with insulin. If the cells were contacted with the candidate agent ***and***

insulin, it would not be possible to determine whether the candidate agent enhances translocation of GLUT4 because translocation would occur due to the presence of insulin. The court has clearly stated that an obviousness rejection based upon the modification of a reference that destroys the intent, purpose or function of the teaching in the reference is not a proper obviousness rejection (*In re Gordon*, 221 U.S.P.Q. 1125 (Fed. Cir. 1984)).

Seed describes "recent applications of bacterial and vertebrate expression cloning systems" (See, page 567, column 1).

The combined teaching of the '924 Patent and Seed would, at most, direct one of skill in the art to use an expression library of candidate agents in the method of the '924 Patent to identify agents which enhance translocation of GLUT4 from an intracellular location to the plasma membrane. However, neither reference suggests or motivates one of skill in the art to include insulin in the method of the '924 Patent since it is known that insulin stimulates GLUT4 translocation. As noted above, if in the method of the '924 Patent, the cells were contacted with an expression library of candidate agents ***and*** insulin, it would not be possible to identify a candidate agent from the library which enhances translocation of GLUT4 because translocation would occur due to the presence of insulin. Including a step in which the cells are contacted with insulin in the method of the '924 Patent would destroy the intent, purpose or function of the method of the '924 Patent. Thus, the obviousness rejection based on the combined teaching of the '924 Patent and Seed is improper.

The combined teaching of the '924 Patent and Seed do not render obvious Applicants' claimed invention.

Objection to Claim 55

Claim 55 is objected to "as being dependent upon a rejected claim, but would be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims" (Office Action, page 6).

Claim 55 has been rewritten in independent form including all the limitations of the base claim and any intervening claims, and thus, is allowable.

## CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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